## REMARKS

Status of the Claims

*Pending claims*

Claims 1 to 30 are pending.

*The Restriction Requirement*

The Patent Office alleged that the pending claims of the application are directed to four separate and distinct inventions because the alleged different inventions or groups of inventions are not so linked as to form a single general inventive concept under PCT Rule 13.1.

Group I: Claims 1-8, 15 and 18-19, drawn to an aziridine compound.

Group II: Claims 9-14 and 16-19, drawn to a complex of an aziridine compound and a methyltransferase.

Group III: Claims 20-29 drawn to a method of modifying a target molecule with an aziridine and a methyltransferase.

Group IV: Claim 30 drawn to a modified molecule.

In response to the Restriction Requirement, Applicants elected Group I, Claims 1 to 8, 15 and 18 to 19, drawn to an aziridine compound, with traverse, respectfully requesting the Patent Office rejoin all claims directed to aziridine compounds (Group I), complexes of aziridine compounds and methyltransferases (Group II) and methods of modifying a target molecule with an aziridine and a methyltransferase (Group III) into one restriction group.

In response to Applicants' response, the Patent Office withdrew, in part, the restriction. Claims 9 to 14 and 16 to 30 were rejoined. Thus, claims 1 to 15 and 20 to 27 are pending and under consideration and claims 16 to 19, 21 to 26 and 28 to 30 are withdrawn from consideration.

*Claims amended and added in the instant amendment*

In the present response, claims 1 to 11, 14 to 19 and 21 to 30 are amended, new claims 31 to 43 are added. Accordingly, after entry of the instant amendment, claims 1 to 43 are pending and under examination.

*Claim objections*

The Patent Office noted that claims 16 to 19, 21 to 26 and 28 to 30 as pending are in improper form. The instant amendment addresses this issue.

*Outstanding Rejections*

Claims 20 to 26 are rejected under 35 U.S.C. §101. Claims 1 to 15 and 27 are rejected under 35 U.S.C. §112, first paragraph. Claims 1 to 15 and 27 to 27 are rejected under 35 U.S.C. §112, second paragraph. Applicants respectfully traverse all outstanding objections to the specification and rejection of the claims.

*Free of the Prior Art*

Applicants thank the Examiner for noting that claims 1 to 15 and 27 appear to be free of the prior art.

Support for the Claim Amendments

The specification sets forth an extensive description of the invention in the new and amended claims. Support for claims directed to compounds having different "n" values can be found, *inter alia*, on page 5, the second, third, fourth and fifth paragraphs.

Issues under 35 U.S.C. §101

Claims 20 to 26 are rejected under 35 U.S.C. §101, because the recitation of a use must set forth steps involved in the process. The instant amendment addresses this issue.

Issues under 35 U.S.C. §112, first paragraph

*Genus of aziridine derivatives*

Claims 1 to 15 and 27 are rejected under 35 U.S.C. §112, first paragraph, for allegedly not enabling how to make and use the claimed genus of aziridine derivatives.

The Patent Office states that the specification does enable claims directed to compounds of the formula 2 and 9 on pages 12 and 16, respectively (i.e., where X is N, Y is N, $R^2$ is H and n is 1 to 4.

However, it is alleged that the specification does not reasonable provide enablement for the broad genus of compounds of formula (I), and in particular, for compounds where X is not N, Y is not N, $R^2$ is not H and n is up to 5000. It is alleged that undue

experimentation is required to determine how to make and use claimed compounds other than compounds of the formula 2 and 9 on page 12 and 16 of the specification, respectively.

With regard to In re Wands' factors (1) and (2), it was alleged that it would take undue experimentation to synthesize the broad genus of claimed species (aziridine derivatives). It was also alleged that it would take undue experimentation to determine if such species are co-factors for a SAM-dependent methyltransferase.

However, as declared by Dr. Elmar Weinhold, using the teaching of the specification, one skilled in the art could have selected from routine methods known in the art at the time of the invention to design synthetic schemes to make any member of the genus of claimed aziridine derivatives. Dr. Weinhold also declares that one skilled in the art could have used routine protocols known in the art at the time of the invention, including those described in the instant specification, to determine if any synthesized specie could act as a co-factor for a SAM-dependent methyltransferase.

Whether large numbers of alternative protocols must be screened to determine if one is within the scope of the claimed invention is irrelevant to an enablement inquiry. Enablement is not precluded by the necessity to screen large numbers of synthetic protocols, as long as that screening is "routine," i.e., not "undue," to use the words of the Federal Circuit. The Federal Circuit in In re Wands directed that the focus of the enablement inquiry should be whether the experimentation needed to practice the invention is or is not "undue" experimentation. The court set forth specific factors to be considered.

One of these factors is "the quantity of experimentation necessary." Guidance as to how much experimentation may be needed and still not be "undue" was set forth by the Federal Circuit in, e.g. Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987). In Hybritech, Inc., a single deposited antibody producing cell line enabled a claim generic to all IgM antibodies directed to a specific antigen. The Federal Circuit noted that the evidence indicated that those skilled in the monoclonal antibody art could, using the state of the art and applicants' written disclosure, produce and screen new hybridomas secreting other monoclonal antibodies falling within the genus without undue experimentation. The court held that applicants' claims need not be limited to the specific, single antibody secreted by the deposited hybridoma cell line (significantly, the

genus of antibodies was allowed even though only one antibody specie was disclosed). The court was acknowledging that, because practitioners in that art are prepared to screen large numbers of negatives in order to find a sample that has the desired properties, the screening that would be necessary to make additional antibody species was not "undue experimentation."

Analogously, one skilled in the synthetic chemistry arts at the time of the instant invention also recognized the need to screen or routinely modify numbers of alternatives to find a protocol that can synthesize any desired specie of the claimed genus of compounds. Furthermore, the screening procedures used to identify if any synthesized specie is a co-factor for a SAM-dependent methyltransferase were all well known in the art at the time this application was filed. All were routine protocols or routine variations of synthetic schemes for the skilled artisan. Thus, the skilled artisan using Applicants' written disclosure could make and use the instant claimed invention without undue experimentation.

With regard to In re Wands' factors (4), (5) and (6), the Patent Office alleges that that there was a great deal of unpredictability in the art, noting, for example, that there was no synthetic method that could have been broadly applied to linking a group comprising one methylene chain as well as linking a group comprising 5000.

However, as noted above and declared by Dr. Weinhold, one skilled in the art using the teaching of the specification and routine methods known in the art at the time of the invention could have designed synthetic schemes to synthesize any member of the claimed genus of aziridine derivatives using only routine screening of alternatives. Even if, *arguendo*, at the time of the invention there was not a known synthetic scheme to make every member of the claimed genus, the specification was still enabling for the claimed genus because it would have taken only routine screening for the skilled artisan to have selected and/or designed the appropriate synthetic scheme to make an aziridine derivative of the present invention.

*Genus of Methyltransferases*

Claims 9, 10 and 13 are rejected under 35 U.S.C. §112, first paragraph, for allegedly not enabling how to make and use a broad genus of methyltransferases. In particular, it was alleged that it would have taken undue experimentation to determine which specific methyltransferase would be able to complex with an aziridine derivative of the present invention.

However, as noted above, enablement is not precluded by the necessity to screen large numbers of alternative compounds, as long as that screening is "routine," i.e., not "undue." As declared by Dr. Weinhold, it would have taken only routine screening to determine if a methyltransferase could have complexed with an aziridine derivative of the present invention. Thus, the specification enabled the skilled artisan at the time of the invention to make and use a broad genus of methyltransferases with an aziridine derivative of the present invention.

With regard to In re Wands' factors (4), (5) and (6), the Patent Office alleges that that there was a great deal of unpredictability in the art noting, inter alia, unpredictability in the structures of methyltransferases, and that the art at the time of the invention fails to establish predictability with regard to how to make and use the aziridine derivatives of the present invention with any methyltransferase.

However, as noted above and declared by Dr. Weinhold, it would have taken only routine screening to select a methyltransferase and determine if it could have complexed with an aziridine derivative of the present invention. Even if, *arguendo*, at the time of the invention it was not known which specific methyltransferase could have complexed with any particular aziridine derivative of the present invention, the specification was still enabling for the claimed invention because it would have taken only routine screening to make this determination.

Accordingly, because the skilled artisan at the time of the invention could have practiced the claimed invention without undue experimentation, the rejection under 35 U.S.C. §112, first paragraph, can be withdrawn.

Issues under 35 U.S.C. §112, second paragraph

Claims 1 to 15 and 27 to 27 are rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite.

*Recitation of a use*

The Patent Office alleges that claims 20 to 26 are indefinite because the claims do not set forth any steps involved in the method or process. The instant amendment addresses this issue.

*The phrase "amino acids which may optionally be modified"*

The Patent Office alleges that claim 1 is indefinite because of the phrase "amino acids which may optionally be modified". The instant amendment addresses this issue.

*The term "derivatives thereof"*

The Patent Office alleges that claim 4 is indefinite because of the term "derivatives thereof". The instant amendment addresses this issue.

*The phrase "electron withdrawing group"*

The Patent Office alleges that claim 1 is indefinite because of the term "electron withdrawing group" because in the absence a particular electron withdrawing group or distinct language and/or chemical formula to decribe a class of compounds that would be considered an "electron withdrawing group", the identity of the "electron withdrawing group" would be difficult to describe.

The second paragraph of 35 USC §112 requires that a specification include claims "particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention." Indefiniteness is a question of law, Carl Zeiss Stiftung v. Renishaw PLC, 945 F.2d 1173, 1181, 20 USPQ2d 1094, 1101 (Fed. Cir. 1991), and determining whether a claim is indefinite requires an analysis of "whether one skilled in the art would understand the bounds of the claim when read in light of the specification. . . . If the claims read in light of the specification reasonably apprise those skilled in the art of the scope of the invention, [section] 112 demands no more." Miles Lab., Inc. v. Shandon Inc., 997 F.2d 870, 875, 27 USPQ2d 1123, 1126 (Fed. Cir. 1993), cert. denied, 114 S. Ct. 943 (1994); see also Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1385, 231 USPQ 81, 94-95 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987).

Applicants respectfully aver that because the phrase "electron withdrawing group" was an art-accepted term at the time of the invention, claims containing this phrase, read in light of the specification and the prior art, reasonably apprise those skilled in the art both of the utilization and scope of the invention. To evidence that the phrase "electron withdrawing group" was an art-accepted term at the time of the invention, Applicants note that a search of the USPTO database for issued U.S. patents with claims containing the term found 929 hits, see

attached Exhibit A, including, for example, the text of U.S. Patent Nos. 5,939,346; 5,985,895; 5,994,391 (partial text, including claim 323); 5,965,566 (partial text, claims only).

Accordingly, because claims containing the phrase "electron withdrawing group", read in light of the specification and the prior art, reasonably apprised those skilled in the art both of the utilization and scope of the invention, the rejection under 35 U.S.C. §112, second paragraph, can be withdrawn.

*The term "small molecule"*

The Patent Office alleges that claim 10 is indefinite because the term "small molecule" in the absence a particular small molecule or distinct language and/or chemical formula to decribe a class of compounds that would be considered a "small molecule", the identity of the term would be difficult to describe.

Applicants respectfully aver that because the phrase "small molecule" was an art-accepted term at the time of the invention, claims containing this phrase, read in light of the specification and the prior art, reasonably apprise those skilled in the art both of the utilization and scope of the invention. To evidence that the phrase "small molecule" was an art-accepted term at the time of the invention, Applicants note that a search of the USPTO database for issued U.S. patents with claims containing the term found 157 hits, see attached Exhibit B, including, for example, the text of U.S. Patent Nos. 5,928,868; 6,010,478; 6,020,096 (claims only).

Accordingly, because claims containing the phrase "small molecule", read in light of the specification and the prior art, reasonably apprised those skilled in the art both of the utilization and scope of the invention, the rejection under 35 U.S.C. §112, second paragraph, can be withdrawn.

## CONCLUSION

In view of the foregoing amendment and remarks, it is believed that the Examiner can properly withdraw the rejection of the pending claims under 35 U.S.C. §112, first and second paragraphs. Applicants believe all claims pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

Applicants believe that no additional fees are necessitated by the present Response. However, in the event any such fees are due, the Commissioner is hereby authorized to charge any such fees to Deposit Account No. 06-1050.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at (858) 678-5070.

Respectfully submitted,

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